

EXHIBIT A115



Original Contribution

Dietary Quality and Ovarian Cancer Risk in African-American Women

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This study evaluated 3 index-based dietary patterns—Healthy Eating Index (HEI)-2005, HEI-2010, and Alternate Healthy Eating Index (AHEI)-2010—in relation to ovarian cancer risk in African-American women. The study was conducted among 415 ovarian cancer cases and 629 age- and site-matched controls of African-American descent recruited from the population-based African American Cancer Epidemiology Study. Multivariable unconditional logistic regression models were used to estimate odds ratios and 95% confidence intervals between quartiles of dietary quality indices and ovarian cancer risk, adjusting for potential confounders. We found that higher AHEI-2010 scores, but not HEI-2005 or HEI-2010 scores, were associated with lower risk of ovarian cancer (comparing the highest quartile (4th) vs. lowest (1st), odds ratio (OR) = 0.66, 95% confidence interval (CI): 0.45, 0.98; *P* for trend = 0.05). When stratified by menopausal status, no noteworthy associations were observed among premenopausal women. However, among postmenopausal women, greater adherence to HEI-2010 (quartile 4 vs. quartile 1, OR = 0.57, 95% CI: 0.36, 0.92; *P* for trend = 0.03) and AHEI-2010 (quartile 4 vs. quartile 1, OR = 0.49, 95% CI: 0.31, 0.78; *P* for trend = 0.01) were inversely associated with ovarian cancer. Our findings indicate that adherence to an overall healthy dietary pattern may reduce ovarian cancer risk in African-American women, and particularly among postmenopausal African-American women.

African Americans; diet; ovarian neoplasms

Abbreviations: AACES, African American Cancer Epidemiology Study; AHEI, Alternate Healthy Eating Index; CI, confidence interval; FFQ, food frequency questionnaire; HEI, Healthy Eating Index; OR, odds ratio.

Ovarian cancer is the fifth leading cause of cancer death among women in the United States (1). Considering the poor survival rates, and that only 10% of cases are from inherited high-risk germline mutations while the rest are thought to be sporadic (2), it would be valuable to identify modifiable life-style factors, including dietary interventions, for ovarian cancer. Compared with assessing single foods or nutrients, the examination of dietary exposures as dietary patterns may better accommodate the multidimensional aspects of diet and more efficiently measure the role of diet in the etiology of ovarian cancer.

Several dietary quality indices, often based on established foods and nutrients predictive of chronic diseases and evidence-based

dietary guidelines, have been developed to reflect the healthfulness of individual overall diet. These indices are meaningful in research settings to understand relationships between dietary patterns and health outcomes. They are also convenient tools for dietitians and physicians to assess personal diet in clinical settings. The Healthy Eating Index (HEI) is a measure of dietary quality based on adherence to the Dietary Guidelines for Americans. Compared with HEI-2005, the updated HEI-2010 has an increased emphasis on dietary quality and reflects the most recent national dietary guidelines (3). Another measure, Alternate Healthy Eating Index–2010 (AHEI-2010), grounded in a different eating guide, the Healthy Eating Pyramid, was based on dietary predictors of chronic diseases (4).

Scores from both HEI-2005 and HEI-2010 were found to predict cardiovascular disease (CVD) and cancer mortality (5). AHEI-2010 scores were found to predict the risk of CVD, diabetes, and cancer (4), which may share etiologic pathways with ovarian cancer, such as inflammation, hyperinsulinemia, and hormonal factors (6, 7). However, whether adherence to any of the dietary recommendations would reduce the risk of ovarian cancer remains unknown. Only 2 studies, conducted in predominantly white populations, examined the HEI-2005 or AHEI-2010 in relation to ovarian cancer risk with insufficient evidence for association (8, 9). To our knowledge, no study has examined the relationship between adherence to the 2010 Dietary Guidelines for Americans (HEI-2010) and ovarian cancer risk. Furthermore, it remains unknown whether adherence to any of the dietary recommendations is associated with a lower risk of ovarian cancer in African Americans who, on average, have lower dietary quality (10) and worse survival from ovarian cancer than their white counterparts (11). Our study was designed to evaluate the association of dietary quality as measured by HEI-2005, HEI-2010, and AHEI-2010 with ovarian cancer risk in African-American women.

METHODS

Design and participants

The African American Cancer Epidemiology Study (AACES) is an ongoing population-based case-control study of ovarian cancer in African-American women in 11 sites in the United States (south- and mid-Atlantic: New Jersey, North Carolina, South Carolina, Georgia; South central: Tennessee, Alabama, Louisiana, Texas; Midwest: Michigan, Illinois, Ohio) (12, 13). Cases were identified by rapid case ascertainment using state cancer registries; Surveillance, Epidemiology, and End Results (SEER) registries; or hospitals' gynecologic oncology departments. Eligible cases included women of self-identified African-American descent aged 20–79 years, who were residents of the defined geographic region for each site, with newly diagnosed (since December 2010) and histologically confirmed invasive epithelial ovarian cancer.

Controls were identified by list-assisted, random-digit dialing, with phone numbers chosen from both landline and cellular telephone exchanges. Women were eligible controls if they self-identified as African Americans, had no previous history of ovarian cancer, and had not had previous bilateral oophorectomy. We aimed to frequency match cases by 5-year age group and state of residence. Anticipated distribution of age and state of residence was provided beforehand to facilitate control accrual. Among those who could be contacted, 66.5% of potential cases and 72% of potential controls agreed to participate in the main telephone interview, which included structured questions on sociodemographic, health, and lifestyle factors. The study was approved by the institutional review boards at all study sites.

The present analyses included 495 cases and 711 controls who completed the telephone interview by December 2014. We excluded 74 cases and 76 controls who did not complete the food frequency questionnaire (FFQ) for dietary assessment, 1 case and 3 controls who reported an extreme

energy intake (greater than twice the interquartile range of log energy intake), and 5 cases and 3 controls with covariates missing, leaving 415 cases and 629 controls in this study. We found no difference with respect to age, education, menopausal status, or other nondietary risk factors listed in Table 1 when comparing women who completed the FFQ with those who did not (data not shown), except for parity, where cases without FFQ were found to have more children (3 children for those without FFQs vs. 2 children for those with FFQs, respectively; $P < 0.001$).

Dietary assessment

Dietary information was obtained via a self-administered Block 2005 FFQ for 110 foods and beverages consumed over the year preceding diagnosis (for cases) or the reference date (for controls). Average daily intakes were calculated by summing the frequency of consumption of a specified serving of food or beverage or by summing the product of the frequency of consumption of a specified serving of food or beverage by the nutrient content of that food or beverage. Average daily total energy intake was estimated as the sum of energy intake across all food and beverage items. Scores for all the indices were calculated using average daily intakes from the FFQ linked to the MyPyramid Equivalents Database 2.0 (US Department of Agriculture) or from published descriptions to generate equivalent intake for nutrients or food groups under each index. Both HEI-2005 and HEI-2010 included 12 food or nutrient components, with total score ranges of 0–100. AHEI-2010 included 10 components with a score range of 0–110. Higher scores indicated better adherence to a healthy diet. The rationale and development details of the indices have been described elsewhere (3, 4). Detailed scoring criteria for the indices are compared in Web Table 1.

Statistical analysis

We compared characteristics between cases and controls using χ^2 tests for categorical variables and t tests to compare means for continuous variables. We also compared scores derived from the 3 index-based dietary patterns using Pearson's correlations.

Because of the frequency matching in our study design, we used unconditional logistic regression models adjusting for the matching factors to estimate odds ratios and 95% confidence intervals. Scores of the 3 indices were categorized into quartiles based on the distributions among controls. The median values of each quartile were treated as a continuous variable to test for linear trends. The 3 dietary indices were also evaluated for each increment of 10 points. The first model adjusted only for age (year) and geographic region (south- and Mid-Atlantic, South central, Midwest). The multivariable-adjusted model further considered a priori the potential confounders or risk factors for ovarian cancer of education (high school or less, some post-high school training, college or graduate degree), parity (0, 1–2, >2), oral contraceptive use (never, <60 months, ≥60 months), menopause status (pre- or postmenopausal), tubal ligation (no,

Table 1. Selected Characteristics of African-American Women Included in the Study, African American Cancer Epidemiology Study, 2010–2014

Characteristic	Cases (n = 415)			Controls (n = 629)			P Value ^a
	No. of Participants	%	Mean (SD)	No. of Participants	%	Mean (SD)	
Age group, years ^b							
20–39	19	4.6		71	11.3		<0.001
40–49	69	16.6		105	16.7		
50–59	150	36.1		237	37.7		
60–69	114	27.5		160	25.4		
70–79	63	15.2		56	8.9		
State of residence ^b							
Michigan or Illinois	40	9.6		93	14.8		0.03
Ohio	31	7.5		60	9.5		
New Jersey	36	8.7		49	7.8		
North Carolina	67	16.1		100	15.9		
South Carolina	56	13.5		51	8.1		
Georgia	73	17.6		130	20.7		
Tennessee or Alabama	45	10.8		64	10.2		
Louisiana	32	7.7		44	7.0		
Texas	35	8.4		38	6.0		
Education							
High school or less	180	44.3		232	36.9		0.05
Some post-high school training	131	32.3		229	36.4		
College or graduate degree	95	23.4		168	26.7		
Parity							
0	81	19.5		83	13.2		0.02
1–2	179	43.1		283	44.9		
>2	155	37.4		263	42.0		
Oral contraceptive use							
Never	120	28.9		123	19.6		0.002
<60 months	167	40.2		284	45.2		
≥60 months	128	30.8		222	35.3		
Postmenopausal	304	73.3		436	69.3		0.17
Ever use of hormone replacement therapy ^c	79	26.3		100	23.0		0.32
Tubal ligation	139	33.5		256	40.7		0.02
Family history of breast/ovarian cancer (first-degree relative)							
No	297	73.2		494	78.5		0.007
Yes	109	26.9		115	18.3		
Unknown	9	2.2		20	3.2		
Body mass index ^d			33.3 (9.0)			32.2 (8.2)	0.03
Total energy intake, kcal			1,783.3 (1,214.4)			1,744.5 (1,127.8)	0.60
Healthy Eating Index–2005, score			61.0 (10.3)			60.9 (10.7)	0.93
Healthy Eating Index–2010, score			61.0 (11.1)			61.7 (11.2)	0.34
Alternate Healthy Eating Index–2010, score			51.7 (10.3)			53.1 (11.1)	0.04

Abbreviation: SD, standard deviation.

^a Student's *t* test for continuous variables and χ^2 tests for categorical variables.^b This study was designed to frequency match controls to cases by 5-year age category and state of residence. The differences in age and state of residence between cases and controls may, in part, be because this is an ongoing study that is still enrolling participants.^c Restricted to postmenopausal women.^d Body mass index was calculated as weight (kg)/height (m)², from measurements 1 year before diagnosis (cases) or reference date (controls).

yes), first-degree family history of breast or ovarian cancer (no, yes), body mass index (weight (kg)/height (m)², calculated from self-reported weight and height 1 year before diagnosis/reference date), physical activity (in the year preceding diagnosis/reference date: 0, <150 minutes/week, ≥150 minutes/week), and total energy intake (kcal). Other potential confounders considered were household income, age at menarche, hormone therapy use, smoking, and history of diabetes, but these were not included in the final model because they affected the estimates for the 3 dietary quality indices by less than 10%.

To explore how each nutrient or food group contributes to the relationship of overall index score and ovarian cancer risk, the independent association between a 1-point increment in score for each index component and risk of ovarian cancer was assessed by simultaneously adjusting for the overall score without the component of interest in the multivariable model.

We examined whether associations between dietary pattern and ovarian cancer risk were modified by menopausal status. Because ovarian cancer is a hormonally related disease, risk factors may have different effects at different stages of life (14). We also assessed whether any associations between diet and ovarian cancer risk were modified by body mass index, physical activity (0, <150 minutes/week, ≥150 minutes/week), or smoking (never, ever) to understand whether diet combined with these lifestyle factors could optimize ovarian cancer prevention. *P*-for-interaction values were obtained via the likelihood ratio test using product terms with quartiles of each of the dietary indices. We also examined the associations by the 2 histological subtypes contributing the largest number of cases (serous and endometrioid) and tested for heterogeneity. Due to stratum sizes, the associations by histological subtypes and the heterogeneity tests were evaluated with the per-10-point increment of the dietary quality score. In the sensitivity analysis, we conducted propensity-score nearest-neighbor matching to further ensure the comparability between cases and controls with respect to our matching criteria (i.e., 5-year age group and state of residence) and repeated the primary analysis among matched samples. Statistical analysis was performed using Stata, version 13.1 (StataCorp LP, College Station, Texas). All statistical tests were 2-sided.

RESULTS

Cases were slightly older than controls and were less likely to reside in the Midwestern states (Michigan, Illinois, and Ohio) (Table 1). Cases were more likely to be nulliparous, to have a family history of breast/ovarian cancer, and to have a higher body mass index. Cases were less likely to have used oral contraceptives or to have had a tubal ligation. Cases were similar to controls in total caloric intake and mean scores on the HEIs but had a lower mean AHEI-2010 score.

Table 2 shows the association of the 3 dietary quality indices with ovarian cancer risk. Higher scores obtained by the AHEI-2010 were associated with lower risk of ovarian cancer in all African-American women. Age- and region-adjusted estimates were similar to results from the multivariable-adjusted

model (highest quartile (4th) vs. lowest (1st), odds ratio (OR) = 0.66, 95% confidence interval (CI): 0.45, 0.98; *P* for trend = 0.05). Each 10-point increase of AHEI-2010 was associated with a 16% decreased odds ratio (95% CI: 0.73, 0.95). Although the AHEI-2010 scores were highly correlated with the HEI-2005 (*r* = 0.74; *P* < 0.001) and HEI-2010 (*r* = 0.77; *P* < 0.001) scores, we observed no significant associations between HEI scores and the risk of ovarian cancer among all women.

We conducted stratified analyses for HEI-2005, HEI-2010, and AHEI-2010 by menopausal status (*P* for interaction = 0.09, 0.056, 0.059, respectively; Table 2). Postmenopausal women had lower risk of ovarian cancer with higher scores of HEI-2010 (quartile 4 vs. quartile 1, OR = 0.57, 95% CI: 0.36, 0.92; *P* for trend = 0.03) and AHEI-2010 (quartile 4 vs. quartile 1, OR = 0.49, 95% CI: 0.31, 0.78; *P* for trend = 0.01). Each 10-point increase of HEI-2010 or AHEI-2010 was associated with a decreased odds ratio—by 17% (95% CI: 0.71, 0.97) or by 25% (95% CI: 0.64, 0.88), respectively. Although we observed a decreased risk for higher HEI-2005 scores among postmenopausal women, the risk estimates were not statistically significant. There was no association between HEI-2005, HEI-2010, or AHEI-2010 and ovarian cancer risk among premenopausal women. The sensitivity analysis using propensity-score matching did not change the observed associations (Web Table 2).

No significant interaction was found for body mass index, physical activity, or smoking. No significant heterogeneity was found when these associations were evaluated by serous or endometrioid histologic subtype for any of the indices (*P* for heterogeneity ≥ 0.15; Web Table 3), but each additional 10 points of AHEI-2010 score was associated with a decreased odds ratio for serous tumors by 22% (95% CI: 0.66, 0.91) among all women and by 31% (95% CI: 0.57, 0.83) among postmenopausal women.

We explored the influence of each food or nutrient component that made up the 3 dietary indices (Table 3). Among postmenopausal women, 3 components of HEI-2010—greens and beans, seafood and plant proteins, and lower intake of empty calories (i.e., calories from solid fats, alcohol and added sugars)—were significantly associated with lower risk of ovarian cancer. Total fruit (including juice) showed positive associations, as reported by others (5). Similar findings for HEI-2005 components can be found in Web Table 4. Two components of AHEI-2010—vegetables and lower intake of sugar-sweetened beverages and fruit juice—showed inverse associations among all women of a similar magnitude. Sugar-sweetened beverages and fruit juice, in particular, were significantly associated with ovarian cancer risk among postmenopausal African-American women.

DISCUSSION

In this population-based study of ovarian cancer among African-American women, AHEI-2010 was associated with a lower risk of ovarian cancer. When stratified by menopausal status, AHEI-2010 and adherence to the current Dietary Guidelines for Americans (i.e., HEI-2010) were both strongly associated with reduced risk of ovarian cancer

Table 2. Odds Ratios for Ovarian Cancer by Quartiles of Dietary Quality Indices Among All Participants and According to Menopausal Status, African American Cancer Epidemiology Study, 2010–2014^{a,b}

Quartile and Menopausal Status ^c	No. of Cases	No. of Controls	Age- and Region-Adjusted		Multivariate-Adjusted ^d	
			OR	95% CI	OR	95% CI
Healthy Eating Index–2005						
All women						
Quartile 1	103	158	1	Referent	1	Referent
Quartile 2	102	158	0.90	0.63, 1.28	0.87	0.60, 1.26
Quartile 3	115	157	1.00	0.70, 1.42	1.03	0.70, 1.50
Quartile 4	95	156	0.82	0.57, 1.18	0.83	0.56, 1.23
P for trend			0.39		0.52	
Per 10-point increase			0.95	0.84, 1.08	0.97	0.84, 1.11
Premenopausal						
Quartile 1	34	65	1	Referent	1	Referent
Quartile 2	27	47	1.00	0.52, 1.94	1.11	0.53, 2.32
Quartile 3	22	47	0.73	0.37, 1.46	0.68	0.31, 1.50
Quartile 4	28	34	1.46	0.74, 2.88	1.24	0.55, 2.78
P for trend			0.51		0.93	
Per 10-point increase			1.11	0.88, 1.39	1.04	0.80, 1.36
Postmenopausal						
Quartile 1	69	93	1	Referent	1	Referent
Quartile 2	75	111	0.85	0.55, 1.31	0.81	0.52, 1.28
Quartile 3	93	110	1.04	0.68, 1.60	1.07	0.68, 1.68
Quartile 4	67	122	0.66	0.43, 1.03	0.68	0.43, 1.10
P for trend			0.14		0.24	
Per 10-point increase			0.89	0.77, 1.03	0.91	0.77, 1.07
Healthy Eating Index–2010						
All women						
Quartile 1	112	159	1	Referent	1	Referent
Quartile 2	110	158	0.88	0.62, 1.25	0.86	0.60, 1.25
Quartile 3	99	158	0.79	0.55, 1.13	0.81	0.55, 1.19
Quartile 4	94	154	0.74	0.51, 1.07	0.74	0.50, 1.11
P for trend			0.09		0.14	
Per 10-point increase			0.90	0.80, 1.01	0.90	0.79, 1.02
Premenopausal						
Quartile 1	36	68	1	Referent	1	Referent
Quartile 2	25	44	0.95	0.49, 1.84	1.00	0.49, 2.05
Quartile 3	22	52	0.69	0.35, 1.35	0.65	0.30, 1.42
Quartile 4	28	29	1.57	0.79, 3.16	1.24	0.54, 2.82
P for trend			0.45		0.94	
Per 10-point increase			1.07	0.87, 1.32	0.99	0.77, 1.28
Postmenopausal						
Quartile 1	76	91	1	Referent	1	Referent
Quartile 2	85	114	0.83	0.54, 1.26	0.80	0.51, 1.23
Quartile 3	77	106	0.78	0.51, 1.21	0.82	0.51, 1.30
Quartile 4	66	125	0.56	0.36, 0.87	0.57	0.36, 0.92
P for trend			0.01		0.03	
Per 10-point increase			0.82	0.71, 0.94	0.83	0.71, 0.97

Table continues

Table 2. Continued

Quartile and Menopausal Status ^c	No. of Cases	No. of Controls	Age- and Region-Adjusted		Multivariate-Adjusted ^d	
			OR	95% CI	OR	95% CI
Alternate Healthy Eating Index–2010						
All women						
Quartile 1	122	159	1	Referent	1	Referent
Quartile 2	98	159	0.79	0.56, 1.12	0.83	0.57, 1.19
Quartile 3	109	155	0.83	0.59, 1.84	0.83	0.57, 1.19
Quartile 4	86	156	0.66	0.46, 0.95	0.66	0.45, 0.98
P for trend			0.04		0.05	
Per 10-point increase			0.85	0.76, 0.96	0.84	0.73, 0.95
Premenopausal						
Quartile 1	29	65	1	Referent	1	Referent
Quartile 2	35	51	1.43	0.75, 2.70	1.69	0.82, 3.47
Quartile 3	22	44	1.09	0.54, 2.18	1.00	0.46, 2.18
Quartile 4	25	33	1.52	0.75, 3.09	0.94	0.40, 2.21
P for trend			0.35		0.63	
Per 10-point increase			1.11	0.89, 1.38	0.94	0.72, 1.21
Postmenopausal						
Quartile 1	93	94	1	Referent	1	Referent
Quartile 2	63	108	0.59	0.38, 0.90	0.60	0.39, 1.93
Quartile 3	87	111	0.73	0.49, 1.10	0.76	0.49, 1.16
Quartile 4	61	123	0.48	0.31, 0.73	0.49	0.31, 0.78
P for trend			0.003		0.01	
Per 10-point increase			0.75	0.65, 0.87	0.75	0.64, 0.88

Abbreviations: AHEI, Alternate Healthy Eating Index; CI, confidence interval; HEI, Healthy Eating Index; OR, odds ratio.

^a *P* for interaction = 0.09, 0.056, and 0.059 for menopausal status with quartiles of HEI-2005, HEI-2010, and AHEI-2010, respectively.

^b *P* for trend was tested by treating the median value of each quartile as a continuous variable in the corresponding logistic regression model.

^c Median score and range from quartile 1 to quartile 4 of HEI-2005: 47.8 (range, 33.3–53.4), 57.6 (range, 53.5–61.0), 64.8 (range, 61.1–69.0), and 73.5 (range, 69.1–88.2); quartile 1 to quartile 4 of HEI-2010: 48.4 (range, 29.8–53.9), 58.4 (range, 54.0–61.9), 65.5 (range, 62.0–69.8), and 75.4 (range, 69.9–91.9); and quartile 1 to quartile 4 of AHEI-2010: 41.4 (range, 27.3–45.4), 49.1 (range, 45.5–51.9), 55.2 (range, 52.0–59.8), and 67.9 (range, 59.9–86.8).

^d Multivariate-adjusted model included age, region, education, parity, oral contraceptive use, menopause status, tubal ligation status, first-degree family history of breast/ovarian cancer, body mass index, physical activity, and total energy intake.

among postmenopausal women. HEI-2005 was not related to ovarian cancer risk.

Our results suggest that, compared with HEI-2005, the recent dietary indices (HEI-2010 and AHEI-2010) can capture aspects of diet more relevant to ovarian cancer. The lower predicted risk with both HEI-2010 and AHEI-2010 among postmenopausal women is as expected considering the 2 indices have several components in common, with emphasis on increasing vegetables, whole fruit, and whole grains and on reducing sodium and added sugar. They also have some distinct differences that may, in part, explain the even stronger associations for AHEI-2010. Compared with HEI-2010, AHEI-2010 gives more weight to fatty acid composition of the diet and does not recommend dairy or total fruit (including fruit juice). While HEI-recommended optimal intake is relative to a

person's total caloric intake, AHEI used an absolute intake approach. Although there is no gold standard for energy adjustment in scoring derivation, which may deserve more research, it is unlikely to meaningfully influence our observations between healthy dietary patterns and a lower risk of ovarian cancer (15). In our study, the individual component results among postmenopausal women were similar to those among all women, while the associations with HEI-2010 total scores (particularly in the highest quartile) and AHEI-2010 were more pronounced in postmenopausal women. These observations comparing total adherence scores versus individual index components likely reflect the advantages of examining dietary pattern as a whole, which could accommodate the complex contributions and interactions from multiple foods and nutrients consumed in combination with varied food preparation

Table 3. Association of Each Component Score of the Healthy Eating Index–2010 and Alternate Healthy Eating Index–2010 With Ovarian Cancer Risk Among All Participants and According to Menopausal Status, African American Cancer Epidemiology Study, 2010–2014

Index and Component	Scoring Criteria		Index-Specific OR (95% CI) ^{a,b}					
	Minimum Score	Maximum Score	Among All Cases/Controls (415/629)		Premenopausal Cases/Controls (111/193)		Postmenopausal Cases/Controls (304/436)	
			OR	95% CI	OR	95% CI	OR	95% CI
Healthy Eating Index–2010 component (maximum points)								
Total vegetables (5), cup eq./per 1,000 kcal	0	≥1.1	0.83	0.73, 0.95	0.72	0.54, 0.96	0.86	0.74, 1.00
Greens and beans (5), cup eq./per 1,000 kcal	0	≥0.2	0.88	0.79, 0.98	0.85	0.68, 1.06	0.87	0.77, 0.99
Total fruit (5) ^c , cup eq./1,000 kcal	0	≥0.8	1.18	1.06, 1.32	1.21	0.96, 1.51	1.19	1.04, 1.35
Whole fruit (5), cup eq./per 1,000 kcal	0	≥0.4	1.04	0.93, 1.16	1.16	0.93, 1.44	0.98	0.86, 1.13
Whole grains (10), oz eq./per 1,000 kcal	0	≥1.5	1.02	0.97, 1.08	1.01	0.90, 1.14	1.03	0.97, 1.09
Dairy (10), cup eq./1,000 kcal	0	≥1.3	1.06	1.00, 1.12	1.10	0.97, 1.25	1.05	0.98, 1.12
Total protein foods (5), oz eq./1,000 kcal	0	≥2.5	0.83	0.68, 1.01	0.59	0.39, 0.88	0.92	0.73, 1.17
Seafood and plant proteins (5), oz eq./1,000 kcal	0	≥0.8	0.86	0.77, 0.97	1.00	0.80, 1.27	0.80	0.70, 0.91
Fatty acids (10), ratio of (PUFAs + MUFAs) to SFAs	<1.2	>2.5	0.97	0.91, 1.03	1.01	0.88, 1.16	0.95	0.89, 1.01
Refined grains (10) ^b , oz eq./1,000 kcal	≥4.3	≤1.8	0.99	0.93, 1.07	0.97	0.84, 1.11	0.99	0.92, 1.08
Sodium (10) ^b , g/1,000 kcal	≥2.0	≤1.1	1.02	0.97, 1.07	1.03	0.94, 1.14	1.01	0.95, 1.08
Empty calories (20) ^{b,d} , % of energy	≥50	≤19	0.96	0.93, 0.99	0.97	0.91, 1.04	0.96	0.92, 0.99
Alternate Healthy Eating Index–2010 component (maximum points)								
Vegetables (10), servings	0	≥5	0.94	0.89, 1.00	0.89	0.78, 1.01	0.96	0.90, 1.03
Nuts and legumes (10), servings	0	≥1	0.98	0.93, 1.03	0.95	0.86, 1.05	0.97	0.92, 1.03
Fruit (10), servings	0	≥4	1.00	0.95, 1.06	0.99	0.88, 1.11	1.00	0.94, 1.06
Whole grains (10), oz eq.	0	≥5	1.04	0.95, 1.13	0.99	0.81, 1.21	1.04	0.94, 1.16
Long-chain (n-3) fats (EPA + DHA) (10), mg	0	250	0.97	0.92, 1.03	0.96	0.85, 1.09	0.96	0.90, 1.04
PUFA (10), % of energy	≤2	≥10	1.00	0.92, 1.08	0.97	0.83, 1.14	1.01	0.92, 1.10
Trans fat (10) ^b , % of energy	≥4	≤0.5	1.12	1.00, 1.24	1.25	0.98, 1.59	1.07	0.94, 1.21
Red/processed meat (10) ^b , servings	≥1.5	0	1.00	0.95, 1.07	1.14	1.00, 1.30	0.95	0.89, 1.03
Sugar-sweetened beverages and fruit juice (10) ^b , servings	≥1	0	0.94	0.90, 0.98	0.99	0.90, 1.08	0.92	0.87, 0.97
Sodium (10) ^b , mg	Highest decile ^e	Lowest decile ^e	1.03	0.97, 1.09	1.08	0.97, 1.20	0.99	0.92, 1.07
Alcohol (10), drinks	≥2.5	0.5–1.5	0.96	0.90, 1.02	0.93	0.82, 1.04	0.97	0.90, 1.05

Abbreviations: CI, confidence interval; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; eq., equivalent; MUFA, monounsaturated fatty acids; OR, odds ratio; PUFA, polyunsaturated fatty acid

^a Model adjusted for age, region, education, parity, oral contraceptive use, menopause status, tubal ligation status, first-degree family history of breast/ovarian cancer, body mass index, physical activity, total energy intake, and the overall index score without the component under study.

^b Estimates for a 1-point increment in score. For components that were reverse scored, higher score indicates lower intake.

^c Total fruit includes fruit juice, whole fruit does not.

^d Calories from solid fats, alcohol and added sugar; threshold for counting alcohol is >13 g/1,000 kcal.

^e Based on a large sample of Block 2005 questionnaires, the 10th and 90th percentiles of sodium intake in women were 1,610 mg/day and 4,138 mg/day, respectively.

methods, as well as alleviating the concern of high correlations between dietary factors in single food or nutrient analysis. In addition, because only the continuous scale was used when evaluating individual index components, any threshold effect may have been overlooked.

To our knowledge, no studies have been published on the association between HEI-2010 and ovarian cancer risk. Our finding of no association between the HEI-2005 and ovarian

cancer risk was consistent with results from both a prospective (8) and a case-control study (9). Of note, findings from the Women's Health Initiative (WHI) suggested that better prediagnosis dietary quality as measured by HEI-2005 was associated with longer survival after a diagnosis of ovarian cancer (16).

To our knowledge, this is the first study to examine the association of AHEI-2010 and ovarian cancer risk in African Americans. In contrast to our finding of reduced risk with higher AHEI-2010

scores, the Nurses' Health Study (among predominantly white US women) found no association (8). The possibility that the associations differ by race/ethnicity is supported by evidence from studies evaluating ovarian cancer risk factors between African Americans and whites (17, 18) and also from studies comparing dietary patterns with other health outcomes in both groups (19, 20). It may be attributed to differences in types and amounts of foods and nutrients consumed (10, 21), cooking methods (21), physiologic mechanisms (22), or other lifestyle correlates (23). Findings from the National Health and Nutrition Examination Survey (NHANES) suggested that African-American adults had lower dietary quality scores as measured by HEI-2005 when compared with their white counterparts (10), which is similar to our observations. For instance, the HEI-2010 scores between the 20th to 80th percentile among African-American controls in our study (scores: 52–72) and in the Southern Community Cohort Study consisting predominantly of African Americans (women's scores: 49–70) (5) are lower than scores from white women studied in the WHI study (scores: 59–75) (24) and from white women in the National Institutes of Health (NIH)-AARP study (scores: 59–76) (25).

We observed that the association between adherence to HEI-2010 or AHEI-2010 and reduced risk of ovarian cancer was evident among postmenopausal but not among premenopausal women. This is consistent with breast cancer studies that found dietary pattern was more predictive of risk for postmenopausal women (26–28). It is possible that for younger women, genetic predisposition is a stronger determinant than lifestyle factors of ovarian cancer. Another possible explanation may be the different distribution of histologic subtypes in pre- and postmenopausal women. For example, serous tumors were more prevalent among postmenopausal women, and it was only among serous tumors that we observed a lower risk of ovarian cancer from higher AHEI-2010 scores. However, a formal heterogeneity test indicated no significant differential association by histologic subtype among all or by menopausal status. Nevertheless, the results among premenopausal women and histologic subtypes should be interpreted cautiously due to small sample sizes and problems of multiple testing.

We recognize the limitations of dietary recall in case-control studies as a result of the diagnosis or of symptoms before diagnosis. To minimize the potential for recall bias, cases were asked to report their diet 1 year before diagnosis, which is beyond the median prediagnostic symptom duration (4 months) for invasive cases (29). If undetected disease influences dietary choices, one might expect to observe more dietary changes for cases with advanced stages. However, we found no difference in any of the 3 indices between cases at early stages vs. advanced stages. In addition, dietary pattern approach has been documented to be a valid and reproducible measure of diet quality (30, 31). It may be more stable over time than tracking individual food or nutrients and therefore subject to less misclassification in retrospective dietary recall. The potential for selection bias is another concern in case-control studies, particularly since we found that women with more children were less likely to have completed the FFQ. However, we found that the distribution of main risk factors among ovarian cancer cases and controls in AACES was similar to that in other studies (23),

which supports the validity of our findings. Another intrinsic limitation of this study is the potential for residual confounding despite adjusting for a wide array of covariates, which did not meaningfully alter the observations.

Despite the challenges provided by the case-control setting, the current study represents the largest sample of African-American ovarian cancer cases and controls available to examine the risk factors in this understudied population. An additional strength is the evaluation of the 3 dietary indices together, which allows direct comparisons among them.

In conclusion, our findings suggest that an overall healthy dietary pattern is associated with lower risk of ovarian cancer. If our results can be confirmed by future studies, this line of inquiry may open up new strategies for preventing ovarian cancer.

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